redox active species, a supporting electrolyte such as tetraheptylammonium tetraphenylborate and various ionophores for $\text{Na}^+$, $\text{K}^+$, $\text{Ca}^{2+}$ and $\text{Cl}^-$). The components were dissolved in tetrahydrofuran (THF) and drop cast onto the electrode, then allowing the THF to evaporate. Reduction of TCNQ or oxidation of decamethylferrocene resulted in selective transfer of a counter ion into the film with Nernstian sensitivity. Beverages, seawater, blood plasma and whole blood were tested for $\text{Na}^+$, $\text{K}^+$ and $\text{Ca}^{2+}$ content and results were in excellent agreement with potentiometric and spectrophotometric techniques. Application of the thin film ISE to screen printed electrodes was achieved by replacing the THF and PVC with dielectric ink.

Dr Alex Harris
email: alexrharris@gmail.com

**Thesis Abstract: Effects of Pneumococcal Vaccination on Otitis Media and Bacterial Carriage in Remote Australian Aboriginal Communities**

**GRANT A. MACKENZIE**

Abstract of a Thesis submitted for the Degree of Doctor of Philosophy, Flinders University, South Australia

**Background**

Populations living in poor socio-economic conditions experience high mortality due to *Streptococcus pneumoniae* infection. Australian Aboriginal people of all ages experience some of the highest recorded rates of pneumococcal infection. Pneumococcal vaccination may prevent pneumococcal infection. However, pneumococcal vaccination programs have had limited introduction and effectiveness, particularly in populations at high risk of disease.

**Areas of research addressed by this thesis**

The focus of this thesis is the effects of pneumococcal vaccines on otitis media (OM) and upper respiratory tract carriage of *S. pneumoniae*. All the studies were undertaken on the Tiwi Islands north of Darwin. Universal infant pneumococcal vaccination combining 3 doses of 7-valent pneumococcal conjugate vaccine (7PCV) and booster 23-valent pneumococcal polysaccharide vaccine (23PPV) began on the Tiwi Islands in late 2001. Using historic comparison data, the effect of this vaccination program for preventing OM was evaluated. Likewise, the effects of vaccination on carriage of *S. pneumoniae*, non-typeable *Haemophilus influenzae*, and *Moraxella catarrhalis* in infants were documented. Studies among Tiwi adults and older children established the prevalence of and risk factors for pneumococcal carriage. The effects of adult pneumococcal polysaccharide vaccination on carriage were studied. Finally, indirect effects of infant pneumococcal vaccination on pneumococcal serotypes carried in older age groups were also explored.

**Contributions to the field of study**

The introduction of universal infant pneumococcal vaccination was associated with small reductions in the rate of severe OM. The clinical significance of these reductions is unclear. By age 12 months, 35% of comparison and 34% of vaccinated participants had experienced tympanic membrane perforation (TMP). Infant pneumococcal vaccination was associated with a non-significant 44% (95% confidence interval [95% CI] -5, 69) reduction in the risk of new episodes of TMP. Vaccinees were significantly less likely to experience perforation of both ears during follow-up compared to comparison participants (Odds ratio [OR]=0.40, 95% CI 0.17, 0.91) and significantly less likely to experience multiple episodes of perforation (OR=0.38,
Despite reduced risk of bilateral and recurrent perforation, similar proportions of comparison and vaccinated participants remained free of perforation. By 12 months of age, 88% of comparison and 89% of vaccinees had experienced acute otitis media. Vaccination was associated with a non-significant 16% (95% CI -17, 42) reduced risk of acute otitis media episodes. Vaccination had no effect on the prevalence of middle ear effusion but was associated with a non-significant 15% (95% CI -20, 40) increase in the time to first middle ear effusion.

Small numbers of perforations from which pathogens were isolated limited statistical comparisons. Among vaccinees, odds of new perforation associated with pneumococcal serotypes included in the 7-valent conjugate vaccine (VT) were non-significantly reduced compared to the comparison group (OR=0.39; 95% CI 0.09, 1.66). Relative to the comparison group, odds of new perforation associated with vaccine-related serotypes (VR) were non-significantly increased in vaccinees (OR=2.65; 95% CI 0.41, 28.9). The proportion of new perforations with serotype 6B was non-significantly reduced in vaccinees compared to the comparison group (OR=0.27; 95% CI 0.02, 1.87).

In the first 18 months of life, vaccinees had reduced carriage of pneumococcal serotypes included in the conjugate vaccine; age 1–3 months (12% versus 33%), age 7–10 months (9% versus 47%), and age 12–17 months (25% versus 56%). The vaccination program was associated with a significant indirect effect of reduced carriage of serotypes included in the 7PCV at 1–3 months of age. Carriage of serotypes unrelated to those in the 7PCV was generally increased in vaccinees. This was not the case among those aged 18–24 months. Increased carriage at less than 17 months of age of serotypes included in the 23PPV but unrelated to 7PCV serotypes was not evident among those aged 18–24 months. Serotype 16F, followed by 19A, emerged as the dominant carriage serotypes. The vaccination program was associated with an indirect effect delaying first acquisition of pneumococcal carriage; median survival time to pneumococcal acquisition was 68 (95% CI 49, 75) days in vaccinated and 52 (95% CI 40, 54) days in comparison participants. The 75% survival time was 90 (95% CI 75, 97) days in vaccinated and 59 (95% CI 53, ∞) days in comparison participants. However, after 12 months of age the prevalence of pneumococcal carriage was unaffected. Significant indirect effects of vaccination delaying acquisition of carriage were not associated with delay in onset of OM in vaccinees (Hazard Ratio=0.85; 95% CI 0.60, 1.20).

Around 25% of Tiwi adults and 68% of those aged 2 to 15 years were carriers of S. pneumoniae. Independent risk factors for carriage among children were young age, a recent runny nose, no recent prescription of antibiotics, the presence of an outside fire at the household, and whether children slept in a room with only other children (rather than a room with adults also). Independent risk factors for carriage among adults were older age, male gender, a recent chest infection, frequently sitting at outside fires, and unemployment. Recent vaccination with 23PPV in Tiwi adults did not appear to reduce carriage of pneumococcal serotypes included in this vaccine. Following introduction of infant pneumococcal vaccination in late 2001, with high coverage and a catch-up program, VT carriage in the unimmunised was unchanged between late 2002 (10%) and early 2004 (10%). Among unimmunised children 2–15 years of age, universal infant pneumococcal vaccination was associated with an indirect effect of reduced carriage of serotypes included in the 7-valent vaccine (comparison versus vaccinated group OR=2.11 (95% CI 1.29, 3.47). Among children 2–15 years of age, a similar proportion of nasal (73%) and nasopharyngeal (61%) swabs detected S. pneumoniae.

**Conclusions**

These studies suggest that among Tiwi infants receiving regular clinical review, the introduction of universal pneumococcal vaccination was associated with reduced risk of recurrent TMP. The clinical benefit of reduced perforation episodes is uncertain though as reductions were limited to recurrent perforation only. There was no change in the cumulative proportion of infants experiencing perforation or acute
otitis media by 12 months of age. Vaccination may have resulted in reduced new perforations associated with VT although the evidence is not strong due to small numbers. Vaccine immunogenicity has resulted in reduced carriage of VT and increased carriage of NVT. As other studies have correlated conjugate vaccination with reduced VT carriage and disease, it seems that appropriate carriage studies may be used to establish vaccine efficacy against VT disease. Temporal changes and participant selection may have biased these results.

Due to continuing high prevalence of severe OM among Aboriginal infants it is recommended that conjugate vaccines of greater valency be introduced as soon as possible. Administration of booster 23PPV at 9 or 12 months of age should also be evaluated. Other interventions aimed at reducing bacterial transmission are needed.

Vaccination was associated with increased carriage of serotypes not included in the 7PCV. Increased carriage of these serotypes was associated with a small non-significant increase in perforation associated with these types relative to the decrease in perforation associated with vaccine serotypes. Replacement carriage and OM does occur, but at present it only partially offsets reduction in perforation associated with vaccine-types.

There is evidence of relatively high pneumococcal carriage prevalence among older age groups of the Tiwi population. Increasing adult age was associated with increased risk of pneumococcal carriage and is also associated with increased rates of invasive disease. Therefore, intervention studies among adults should consider carriage as an outcome measure. Carriage studies among older children in remote Aboriginal communities, and similar populations, may use nasal rather than nasopharyngeal specimens with similar rates of detection of pneumococcal carriage. Vaccination of Tiwi adults with 23PPV did not reduce carriage of serotypes included in the vaccine. Other studies suggesting poor efficacy in certain populations suggest that 23PPV should be formally evaluated in Aboriginal adults. Finally, universal infant pneumococcal vaccination had an indirect effect among older Tiwi children whereby carriage of serotypes included in the 7PCV was reduced. With introduction of infant pneumococcal vaccination where high coverage is achieved and where catch-up vaccination is performed, immediate and indirect effects on carriage in the unimmunised population need only be assessed with a single post-introduction survey. Potentially increased indirect beneficial effects of greater valency conjugate vaccines and common pneumococcal antigen vaccines should stimulate clinicians, public health organisations, and researchers to advocate for their further development and licensure.

View This Item Online: https://www.biodiversitylibrary.org/item/174356
DOI: https://doi.org/10.5962/p.361601
Permalink: https://www.biodiversitylibrary.org/partpdf/361601

Holding Institution
Smithsonian Libraries

Sponsored by
Biodiversity Heritage Library

Copyright & Reuse
Copyright Status: In Copyright. Digitized with the permission of the rights holder
Rights Holder: Royal Society of New South Wales
License: http://creativecommons.org/licenses/by-nc-sa/3.0/
Rights: https://www.biodiversitylibrary.org/permissions/

This document was created from content at the Biodiversity Heritage Library, the world's largest open access digital library for biodiversity literature and archives. Visit BHL at https://www.biodiversitylibrary.org.

This file was generated 27 June 2023 at 12:04 UTC